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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/460,216	12/13/1999	GRAHAM P. ALLAWAY	50875-F-PCT-	2202

7590 10/17/2006

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EXAMINER	
PARKIN, JEFFREY S	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/460,216	ALLAWAY, G. P., ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/07/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communication filed 07 August, 2006. Claim 61 is pending and claims 1-60 and 62-65 have been canceled without prejudice or disclaimer.

35 U.S.C. § 112, Second Paragraph

The previous rejection of claim 61 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is hereby withdrawn in response to applicants' amendment.

37 C.F.R. § 1.98

The Information Disclosure Statement filed 07 August, 2006, has not been fully considered. This submission cites approximately 282 documents requiring a listing on a 19 page PTO-1449. In an initial review of 10 U.S. patents and published applications, the Office finds that only 1 of these documents is material to patentability of one or more claims in accordance with 37 C.F.R. § 1.56. In view of the very low percentage of references material to patentability in the sampled documents reviewed, the submission is not in compliance with 37 C.F.R. § 1.56 and 1.98. Accordingly, the remaining references will not be considered.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the

invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

Claim 61 stands rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 U.S.P.Q.2d 1398, (Fed. Cir. 1997). *Fiers v. Revel Co.*, 984 F.2d 1164, 25 U.S.P.Q.2d 1601, (Fed. Cir. 1993). *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 U.S.P.Q.2d 1016, (Fed. Cir. 1991). *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 296 F.3d 1316, 63 U.S.P.Q.2d 1609, (Fed. Cir. 2002). *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). *University of Rochester* v. *G. D. Searle & Co., Inc.*, 358 F.3d 916, 69 U.S.P.Q.2d 1886 (C.A.F.C. 2004). The claim is directed toward a method of inhibiting HIV-1 macrophage-tropic infection of a $CD4^+$ cell by contacting said cell with an **agent** that is capable of binding to cell surface CCR5. The claim also stipulates that said agent blocks $HIV\text{-}1_{JR\text{-}FL}$ fusion with a PM-1 cell while not affecting fusion of the $HIV\text{-}1_{BRU}$ with the same cell type.

As previously set forth, to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had **possession** of the claimed invention. See, e.g., *Vas-Cath, Inc., v. Mahurkar*, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116. The issue raised in this application is whether the original application provides adequate support for

the broadly claimed genus of **agents** that are capable of abrogating HIV-1 infection by binding to the CCR5 chemokine receptor. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, **structures**, figures, diagrams, and **formulas** that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). **The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence** described only by functional characteristic, **without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the biomolecule of interest.** *In re Bell*, 991 F.2d 781, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993). *In re Deuel*, 51 F.3d 1552, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995). A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 U.S.P.Q.2d 1895, 1905 (Fed. Cir. 1995). **The court noted in this decision that a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not reasonably lead those skilled in the art to any particular species.**

An applicant may show possession of an invention by disclosure of drawings or **structural chemical formulas** that are sufficiently detailed to show that applicant was in **possession** of the claimed

invention as a whole. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., **complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.** For some biomolecules, examples of identifying characteristics include a nucleotide or **amino acid sequence, chemical structure, binding affinity,** binding specificity, and molecular weight. **The written description requirement may be satisfied through disclosure of function and** minimal structure when there is a well-established correlation **between structure and function.** Without such a correlation, the capability to recognize or understand the structure form the mere recitation of function and minimal structure is highly unlikely. In the latter case, **disclosure of function alone is little more than a wish for possession; it does not satisfy the written description requirement.** *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1566, 43 U.S.P.Q.2d 1398, 1404, 1406 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998). *In re Wilder*, 736 F.2d 1516, 1521, 222 U.S.P.Q. 369, 372-3 (Fed. Cir. 1984). Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.

The claim of the instant application is still broadly directed toward **any agent** that is capable of abrogating HIV-1 infection through CCR5 binding interactions. The claim does not limit the genus to any particular type of compound (i.e., peptidyl, organic,

fatty acid, etc.) or any particular family of compounds (small molecular weight peptidyl inhibitors, antibody-based reagents, etc.). The disclosure provides a generic *in vitro* resonance energy transfer (RET) screening assay that enables the skilled artisan to detect HIV-1 fusion events. This method by itself does not lead the skilled artisan to any particular class of compounds. The disclosure also fails to provide sufficient structural/functional guidance pertaining to suitable compounds that can reasonably be expected to function in the claimed methodology. Thus the genus corresponding to the agent employed in the claimed assay encompasses an inordinate number of unrelated species (e.g., proteins, oligopeptides, retroinverso oligopeptides, polyclonal antibodies, monoclonal antibodies, chimeric antibodies, small molecule inhibitors, etc.). It is noted that some data was supplied pertaining to a limited number of agents from two subgenuses. Specifically, a small number of β-chemokines were identified with inhibitory activity (e.g., the **β-chemokines MIP-1α** and **-1β**). These two chemokines are natural ligands for the CCR5 receptor. A second group was identified including a small and limited number of **CCR5-specific monoclonal antibodies** (e.g., **PA-9-12**). Appropriate amendment of the claim language to incorporate these two subgenuses would obviate the rejection (i.e., "...contacting the cell with a CCR5-specific monoclonal antibody selected from the group consisting of PA-9, PA-10, PA-11, and PA-12" or "...contacting the cell with a β-chemokine selected from the group consisting of MIP-1α and -1β").

Although the specification does provide a small number of inhibitory agents, nevertheless, this limited number of species are insufficient to place the inventors in possession of the full genus of agents at the time of filing. First, the disclosure fails to provide any significant structural information concerning the molecular determinants (i.e., epitopes, structural domains, etc.)

on CCR5 that modulate CCR5-CD4-gp120 binding events. Thus, the skilled artisan would not be able to perform any type of rational drug-screening approach. Instead, putative antiviral agents would need to be identified through trial-and-error. Second, the disclosure fails to provide adequate guidance pertaining to the structures of any particular subgenus of inhibitory agents. The disclosure fails to provide any useful structural criteria for small molecule inhibitors, peptidomimetics, retroinverso polypeptides, antigen-antibody binding sites, etc. Thus, the skilled artisan cannot readily envisage the structure of any particular putative antiviral agent. Third, although the specification provides a generic screening assay to identify potential candidate molecules, nevertheless, this assay fails to lead the skilled artisan to any particular subgenus of inhibitory agent. Applicants are essentially relying upon others to identify putative antiviral agents that would meet the claim limitations. Fourth, the state-of-the-art as it pertains to HIV antiviral development is characterized by unpredictability. The CCR5 chemokine receptor is a large transmembrane spanning protein. It interacts with both gp120 and CD4 during virion-cell fusion events. These interactions may employ linear domains or conformational domains. However, the precise determinants modulating these binding interactions remain to be elucidated. Accordingly, it would be difficult for the skilled artisan to identify candidate agents because of the dearth of structural information. For instance, if the skilled artisan was employing a peptidomimetic, what is the appropriate amino acid sequence of said mimetic? If the skilled artisan is going to employ a small molecule organic inhibitor, what is the structure of this compound? The disclosure fails to address these concerns. Accordingly, the skilled artisan would reasonably conclude that applicants were not in possession of the claimed genus of compounds at the time of filing.

Response to Arguments

Applicants traverse the rejection and again submit that the disclosure would lead the skilled artisan to conclude that applicants were in full possession of the claimed invention at the time of filing. Applicants maintained that the pending claim is not directed toward an agent, but rather a method of inhibiting macrophage tropic HIV-1 infection of $CD4^+$ cells, suggesting that the written description criteria relied upon are not applicable in this situation. Applicants are again directed toward *University of Rochester* v. *G. D. Searle & Co., Inc.*, 358 F.3d 916, 69 U.S.P.Q.2d 1886 (C.A.F.C. 2004), wherein the court concluded that the written description requirement applies equally to both product and method claims. The court unambiguously stated that a "patent directed to method for inhibiting prostaglandin synthesis in human host using unspecified compound,...,is subject to written description requirement,...,since requirement applies to all inventions, including chemical inventions involving nongenetic materials, and since fact that patent is directed to method entailing use of compound, rather than to compound per se, does not remove patentee's obligation to provide description of compound sufficient to distinguish infringing methods from noninfringing methods." The facts in this situation are similar to the facts in the instant application. Applicants are claiming a method that employs a poorly defined agent. The agent is described solely in functional terms without any accompanying meaningful structural limitations. The court also noted that "Even with the three-dimensional structures of enzymes such as COX-1 and COX-2 in hand, it may even now not be within the ordinary skill in the art to predict what compounds might bind to and inhibit them, let alone have been within the purview of one of ordinary skill in the art in the 1993-1995 period". Thus, the skilled artisan would reasonably conclude that applicants were not in possession of the full genus of agents at the time of filing.

It was again maintained that since the level of skill in the art was high, the level of disclosure required to meet the written description requirement is considerably less. The examiner does not concur with this assessment. The effective filing year of the application is 1996. Contrary to applicants' assertion, the design of HIV antiviral agents was a difficult undertaking (Gait and Karn, 1995; Richman, 1996; Mellors, 1996; Back, 1999). As Gait and colleague (1995) conclude, "There can be few tasks in biotechnology that are more challenging than designing antiviral drugs...early protease inhibitors tended to suffer from problems of short serum half-life, poor bioavailability and rapid clearance...new difficulties have emerged from the resultant clinical experience, such as sequestration of the drug by serum proteins, drug resistance and uneven tissue distribution throughout the body. Since these types of problems are unpredictable, it remains necessary to take into account the pharmacological parameters in any drug development programme at the earliest possible stage." Clearly the generation of efficacious antivirals is not a facile undertaking.

Applicants also argue that since they provided a screening assay for identifying agents with the desired properties, they clearly were in possession of the claimed invention. This argument is also inapposite. As set forth *supra*, the court in *Univ. of Rochester* clearly established that simply providing a generic methodology was insufficient to meet the written description requirement without some significant structural/functional nexus. Simply having a screening assay does not allow the skilled artisan to readily envisage the structure of any given agent with the desired functional properties. The disclosure needs to provide a more detailed structural and functional analysis.

Thus, the skilled artisan would reasonably conclude that applicants were not in possession of the full genus of agents at the time of filing.

Finality of Office Action

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). **A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.**

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Bruce R. Campell, Ph.D., can be reached at (571) 272-0974. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related

Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

15 October, 2006